

PATENT  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Masanobu SUGAWARA et al.

Serial Number: Not Yet Assigned  
(PCT/JP01/01132)

Filed: October 17, 2001

For: PROCESS FOR PRODUCING OPTICALLY ACTIVE AMINO ACID  
DERIVATIVES

PRELIMINARY AMENDMENT

Commissioner for Patents  
Washington, D.C. 20231

October 17, 2001

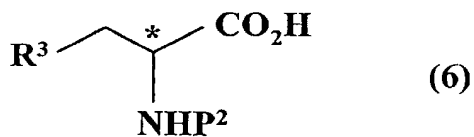
Sir:

Prior to the calculation of the filing fees of the above application, please amend the application as follows:

IN THE CLAIMS:

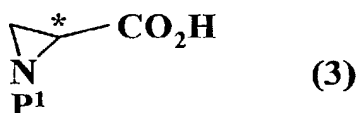
Please amend the following claims as follows:

7. (Amended) A process for producing an optically active amino acid derivative represented by the following formula (6):



wherein R<sup>3</sup> represents an optionally substituted cyclic or noncyclic alkyl group having 1 to 30 carbon atoms, an optionally substituted aralkyl group having 7 to 30 carbon atoms, an optionally substituted aryl group having 6 to 30 carbon atoms, an optionally substituted alkenyl group having 2 to 30 carbon atoms, or an optionally substituted alkynyl group having 2 to 30 carbon atoms; and P<sup>2</sup> has the same meaning as P<sup>1</sup> as described above or represents a hydrogen atom;

or its salt characterized by comprising treating an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3) which is produced by a method as claimed in claims 1, 2, 4 or 5 :



wherein P<sup>1</sup> and \* are each as defined above;

or its salt with an organic metal reagent represented by the following formula (5):



wherein R<sup>3</sup> is as defined above; and M represents an atomic group containing an alkali metal atom or an alkaline earth metal atom or an atomic group containing a zinc ion;

followed by, if needed, deblocking.

9. (Amended) A production process as claimed in claim 7, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):

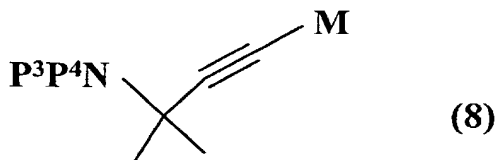


wherein  $R^4$  represents an optionally substituted alkyl group having 1 to 30 carbon atoms, an optionally substituted aralkyl group having 7 to 30 carbon atoms, or an optionally substituted aryl group having 6 to 30 carbon atoms;

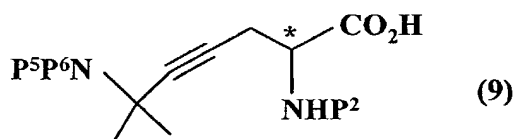
to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

11. (Amended) A production process as claimed in claim 7, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

13. (Amended) A production process as claimed in claim 7, wherein a metal acetylide represented by the following formula (8):



wherein M is as defined above; and P<sup>3</sup> and P<sup>4</sup> independently represent each a hydrogen atom or an amino-protective group, or P<sup>3</sup> and P<sup>4</sup> form together an amino-protective group;  
 is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):



wherein P<sup>5</sup> and P<sup>6</sup> independently have the same meanings as P<sup>3</sup> and P<sup>4</sup> as described above; P<sup>2</sup> has the same meaning as P<sup>2</sup> as defined in the above formula (6); and \* represents the position of an asymmetric carbon atom; or its salt as the compound represented by the formula (6).

15. (Amended) A production process as claimed in claim 13, wherein P<sup>3</sup> and P<sup>4</sup> in the formulae (8) and (10) respectively represent a hydrogen atom and a benzyl group.

19. (Amended) A production process as claimed in claim 16 or 17, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):

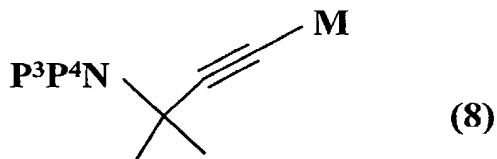


wherein R<sup>4</sup> is as defined above;

to give a compound represented by the formula (6) wherein P<sup>2</sup> is a hydrogen atom.

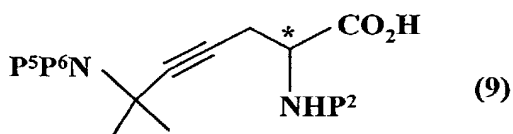
21. (Amended) A production process as claimed in claim 16 or 17, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

23. (Amended) A production process as claimed in claim 16 or 17, wherein a metal acetylide represented by the following formula (8):



wherein M,  $P^3$  and  $P^4$  are each as defined above;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):

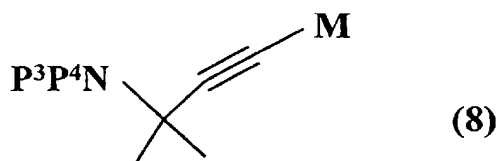


wherein  $P^2$ ,  $P^5$ ,  $P^6$  and \* are each as defined above;

or its salt as the compound represented by the formula (6).

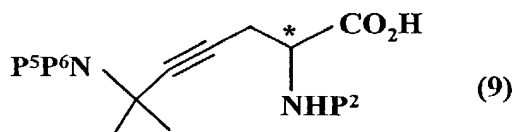
25. (Amended) A production process as claimed in claim 23, wherein  $P^3$  and  $P^4$  in the formula (8) respectively represent a hydrogen atom and a benzyl group.

32. (Amended) A production process as claimed in claim 26 or 27, wherein a metal acetylide represented by the following formula (8):



wherein  $M$ ,  $P^3$  and  $P^4$  are each as defined above;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):



wherein  $P^2$ ,  $P^5$ ,  $P^6$  and  $*$  are each as defined above;

or its salt as the compound represented by the formula (6).

34. (Amended) A production process as claimed in claim 32, wherein  $P^3$  and  $P^4$  in the formula (8) respectively represent a hydrogen atom and a benzyl group.

38. (Amended) A production process as claimed in claim 35 or 36, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):

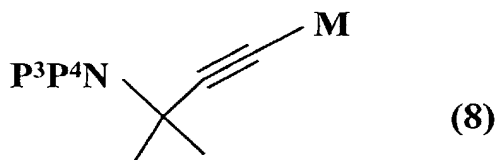


wherein  $R^4$  is as defined above;

to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

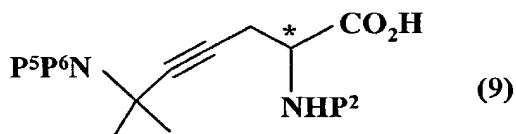
40. (Amended) A production process as claimed in claim 35 or 36, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

42. (Amended) A production process as claimed in claim 35 or 36, wherein a metal acetylide represented by the following formula (8):



wherein M, P<sup>3</sup> and P<sup>4</sup> are each as defined above;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):

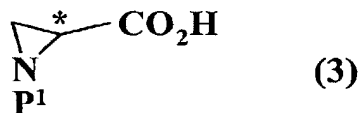


wherein P<sup>2</sup>, P<sup>5</sup>, P<sup>6</sup> and \* are each as defined above;

or its salt as the compound represented by the formula (6).

44. (Amended) A production process as claimed in claim 42, wherein P<sup>3</sup> and P<sup>4</sup> in the formula (8) respectively represent a hydrogen atom and a benzyl group.

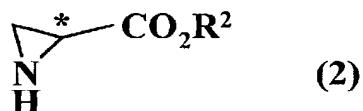
50. (Amended) A process for producing an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3):



wherein P<sup>1</sup> and \* are each as defined above;



or its salt characterized by comprising treating an optically active aziridine-2-carboxylic acid derivative represented by the following formula (2) which is produced by a method as claimed in claim 45 or 46:

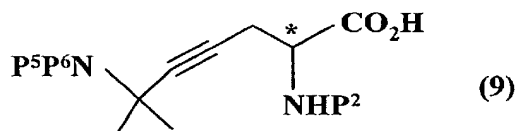


wherein R<sup>2</sup> and \* are each as defined above;

with benzenesulfonyl chloride p substituted by nitro at the 2- and/or 4-positions followed by, if needed, ester hydrolysis.

62. (Amended) A crystallization process as claimed in any of claims 57 to 59, wherein the reaction is performed in the coexistence of an organic solvent compatible with water.

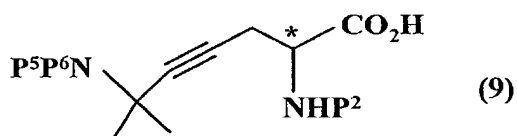
63. (Amended) A crystallization process as claimed in any of claims 57 to 59, wherein said compound represented by the formula (6) is an N-protected optically active amino acid derivative salt represented by the following formula (9):



wherein P<sup>2</sup> represents a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group; and P<sup>5</sup>, P<sup>6</sup> and \* are each as defined above.

67. (Amended) A crystallization process as claimed in claim 64 or 65, wherein the reaction is performed in the coexistence of an organic solvent compatible with water.

68. (Amended) A crystallization process as claimed in claim 64 or 65, wherein said compound represented by the formula (6) is an optically active amino acid derivative salt represented by the following formula (9):



wherein P<sup>2</sup> represents a hydrogen atom; and P<sup>5</sup>, P<sup>6</sup> and \* are each as defined above.

REMARKS

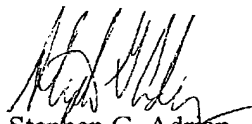
The above amendment is believed to place the claims in proper condition for examination.  
Early and favorable action is awaited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

In the event there are any additional fees required, please charge our Deposit Account No. 01-2340.

Respectfully submitted,

ARMSTRONG, WESTERMAN, HATTORI,  
McLELAND & NAUGHTON, LLP



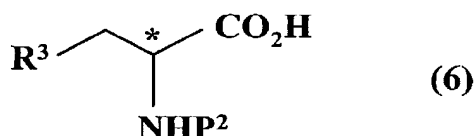
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

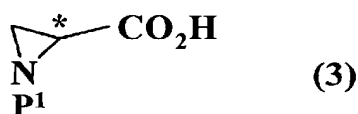
The following claims have been amended as follows:

7. (Amended) A process for producing an optically active amino acid derivative represented by the following formula (6):



wherein R<sup>3</sup> represents an optionally substituted cyclic or noncyclic alkyl group having 1 to 30 carbon atoms, an optionally substituted aralkyl group having 7 to 30 carbon atoms, an optionally substituted aryl group having 6 to 30 carbon atoms, an optionally substituted alkenyl group having 2 to 30 carbon atoms, or an optionally substituted alkynyl group having 2 to 30 carbon atoms; and P<sup>2</sup> has the same meaning as P<sup>1</sup> as described above or represents a hydrogen atom;

or its salt characterized by comprising treating an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3) which is produced by a method as claimed in ~~any of~~ claims 1, 2, 4 or 5:



wherein P<sup>1</sup> and \* are each as defined above;

or its salt with an organic metal reagent represented by the following formula (5):



wherein  $R^3$  is as defined above; and M represents an atomic group containing an alkali metal atom or an alkaline earth metal atom or an atomic group containing a zinc ion; followed by, if needed, deblocking.

9. (Amended) A production process as claimed in claim 7 ~~or 8~~, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):

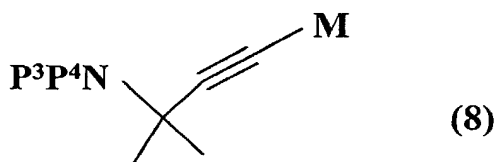


wherein  $R^4$  represents an optionally substituted alkyl group having 1 to 30 carbon atoms, an optionally substituted aralkyl group having 7 to 30 carbon atoms, or an optionally substituted aryl group having 6 to 30 carbon atoms;

to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

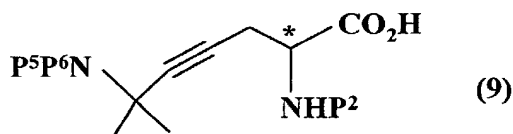
11. (Amended) A production process as claimed in claim 7 ~~or 8~~, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

13. (Amended) A production process as claimed in ~~any of claims 7 to 12~~ claim 7, wherein a metal acetylide represented by the following formula (8):



wherein M is as defined above; and  $P^3$  and  $P^4$  independently represent each a hydrogen atom or an amino-protective group, or  $P^3$  and  $P^4$  form together an amino-protective group;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):



wherein  $P^5$  and  $P^6$  independently have the same meanings as  $P^3$  and  $P^4$  as described above;  $P^2$  has the same meaning as  $P^2$  as defined in the above formula (6); and \* represents the position of an asymmetric carbon atom; or its salt as the compound represented by the formula (6).

15. (Amended) A production process as claimed in claim 13 or 14, wherein  $P^3$  and  $P^4$  in the formulae (8) and (10) respectively represent a hydrogen atom and a benzyl group.

19. (Amended) A production process as claimed in ~~any of claims 16 to 18~~ claim 16 or 17, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):

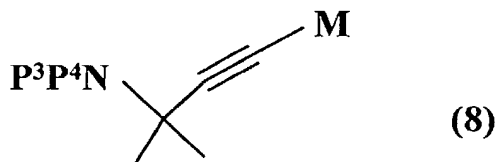


wherein  $R^4$  is as defined above;

to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

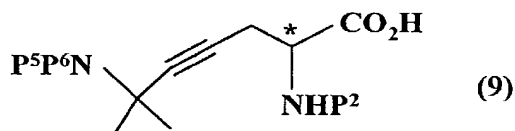
21. (Amended) A production process as claimed in ~~any of claims 16 to 18~~ claim 16 or 17, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein  $P^2$  is a hydrogen atom.

23. (Amended) A production process as claimed in ~~any of claims 16 to 22~~ claim 16 or 17, wherein a metal acetylide represented by the following formula (8):



wherein M, P³ and P⁴ are each as defined above;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):

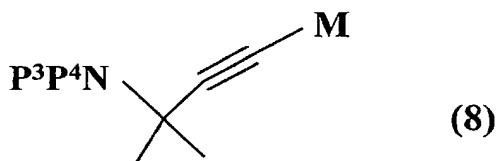


wherein P², P⁵, P⁶ and \* are each as defined above;

or its salt as the compound represented by the formula (6).

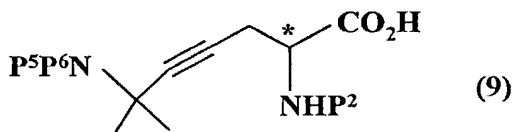
25. (Amended) A production process as claimed in claim 23 ~~or 24~~, wherein P³ and P⁴ in the formula (8) respectively represent a hydrogen atom and a benzyl group.

32. (Amended) A production process as claimed in ~~any of claims 26 to 31~~ claim 26 or 27, wherein a metal acetylide represented by the following formula (8):



wherein M, P<sup>3</sup> and P<sup>4</sup> are each as defined above;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):



wherein P<sup>2</sup>, P<sup>5</sup>, P<sup>6</sup> and \* are each as defined above;

or its salt as the compound represented by the formula (6).

34. (Amended) A production process as claimed in claim 32 ~~or 33~~, wherein P<sup>3</sup> and P<sup>4</sup> in the formula (8) respectively represent a hydrogen atom and a benzyl group.

38. (Amended) A production process as claimed in ~~any of claims 35 to 37~~ claim 35 or 36, wherein said deblocking is performed with the use of a thiol compound represented by the following formula (7):



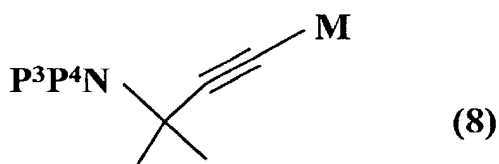
wherein R<sup>4</sup> is as defined above;

to give a compound represented by the formula (6) wherein P<sup>2</sup> is a hydrogen atom.



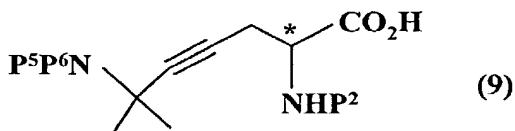
40. (Amended) A production process as claimed in ~~any of claims 35 to 37~~ claim 35 or 36, wherein said deblocking is performed with the use of a metal alkoxide to give a compound represented by the formula (6) wherein P<sup>2</sup> is a hydrogen atom.

42. (Amended) A production process as claimed in ~~any of claims 35 to 41~~ claim 35 or 36, wherein a metal acetylide represented by the following formula (8):



wherein M, P<sup>3</sup> and P<sup>4</sup> are each as defined above;

is used as said organic metal reagent represented by the formula (5) to give an optically active amino acid derivative represented by the following formula (9):

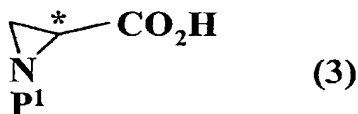


wherein P<sup>2</sup>, P<sup>5</sup>, P<sup>6</sup> and \* are each as defined above;

or its salt as the compound represented by the formula (6).

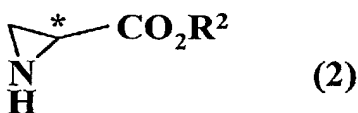
44. (Amended) A production process as claimed in claim 42 ~~or 43~~, wherein P<sup>3</sup> and P<sup>4</sup> in the formula (8) respectively represent a hydrogen atom and a benzyl group.

50. (Amended) A process for producing an optically active N-protected-aziridine-2-carboxylic acid represented by the following formula (3):



wherein P<sup>1</sup> and \* are each as defined above;

or its salt characterized by comprising treating an optically active aziridine-2-carboxylic acid derivative represented by the following formula (2) which is produced by a method as claimed in any of claims 45 to 49 claim 45 or 46:

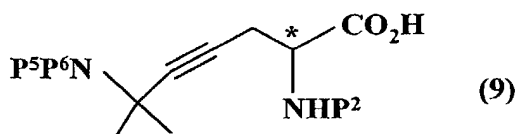


wherein R<sup>2</sup> and \* are each as defined above;

with benzenesulfonyl chloride p substituted by nitro at the 2- and/or 4-positions followed by, if needed, ester hydrolysis.

62. (Amended) A crystallization process as claimed in any of claims 57 to 61 59, wherein the reaction is performed in the coexistence of an organic solvent compatible with water.

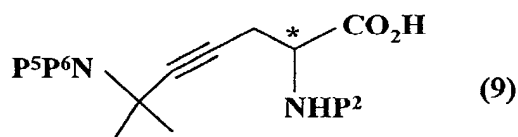
63. (Amended) A crystallization process as claimed in any of claims 57 to 62 59, wherein said compound represented by the formula (6) is an N-protected optically active amino acid derivative salt represented by the following formula (9):



wherein P<sup>2</sup> represents a 2-nitrobenzenesulfonyl group or a 4-nitrobenzenesulfonyl group; and P<sup>5</sup>, P<sup>6</sup> and \* are each as defined above.

67. (Amended) A crystallization process as claimed in ~~any of claims 64 to 66~~ claim 64 or 65, wherein the reaction is performed in the coexistence of an organic solvent compatible with water.

68. (Amended) A crystallization process as claimed in ~~any of claims 64 to 67~~ claim 64 or 65, wherein said compound represented by the formula (6) is an optically active amino acid derivative salt represented by the following formula (9):



wherein P<sup>2</sup> represents a hydrogen atom; and P<sup>5</sup>, P<sup>6</sup> and \* are each as defined above.